REMARKS

Claims 1, 2, 6, and 8 are pending. Claim 1 has been amended to incorporate the features of claim 3 and to recite the specific biological targets disclosed at paragraph [0052] of the published U.S. application (i.e., 2008/0044350). Claim 1 has also been amended to specify that the contrast agent comprises a cyanine dye as set forth in paragraph [0091] of the published U.S. application. Claims 2, 6, and 8 have been amended to comport with the amendments to claim 1. No new matter has been introduced by way of the amendments to the foregoing claims. Claims 3-5, 7, and 9-13 have been cancelled. Applicant reserves the right to file one or more divisional applications to pursue the subject matter of the cancelled claims.

I. *The rejection of claims 1-9 and 12 under 35 U.S.C. § 112, first paragraph (written description) should be withdrawn*

Claims 1-9 and 12 stand rejected under 35 U.S.C. § 112, first paragraph (written description) for the reasons set forth on pages 2 and 3 of the Office Action. While not acquiescing to the Patent Office's position with regard to original claims 1-9 and 12, and simply in an effort to expedite the prosecution of the instant application, Applicants have amended claim 1, from which all the other pending claims depend, to incorporate the structure that was allegedly missing from that claim. For example, as amended, claim 1 provides that V is one or more vector moieties that target COX-2, urokinase receptor, epidermal growth factor receptor or vascular endothelial growth factor receptor (VEGFR). Claim 1 also specifies that the reporter moiety, R, comprises a cyanine dye. Applicants respectfully assert that the amendments to claim 1 overcome the rejection under 35 U.S.C. § 112, first paragraph (written description) because they provide the structure that was allegedly missing from that claim. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

II. *The rejection of claims 1-9 and 12 under 35 U.S.C. § 102(b) should be withdrawn*

Claims 1-9 and 12 stand rejected under 35 U.S.C. 102(b) over Weissleder *et al* (US 2003/0044353 A1) and Lauffer *et al* (US 2002/0034476 A1) for the reasons set forth on pages 4-7 of the Office Action. Applicants respectfully traverse this rejection.

It is axiomatic that a prior art reference anticipates a claim if "each and every limitation is found either expressly or inherently in [that] single prior art reference." *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1360 (Fed. Cir. 1998). In addition, "unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102. *Net Moneyin, Inc. v. Verisign, Inc.*, 549 F.3d 1359, 1371 (Fed. Cir. 2008). Applicants submit that the "four corners" of Weissleder and Lauffer do not disclose all of the limitations arranged or combined in the same way as recited in amended claim 1. Accordingly, neither Weissleder nor Lauffer anticipate claim 1 or any of the claims that depend therefrom. Reconsideration and withdrawal of these rejections are therefore respectfully requested.

Claim 1, as amended, is directed to an agent of formula V-L-R where V is one or more vector moieties that target COX-2, urokinase receptor, epidermal growth factor receptor or vascular endothelial growth factor receptor (VEGFR); L is a linker moiety or a bond; and R comprises a cyanine dye.

Weissleder provides an extremely generic disclosure directed to "activatable" imaging probes that include a chromophore attachment moiety and one or more chromophores chemically linked to the chromophore attachment moiety. Weissleder abstract. Weissleder provides that the attachment moiety can be "any biocompatible polymer." Weissleder at paragraph [0042]. Such polymers include polypeptides such as poly(L-lysine) or polygylcolic acid. *Id.* In some embodiments, Weissleder's probes can contain "specific target binding sites," including "peptide substrates." *Id.* at paragraph [0088]. Such "peptide substrates" include "cathepsin B-specific peptide substrates, MMP substrates, and thrombin substrates." *Id.* at paragraph [0089]. In the examples, Weissleder discloses three specific

near-infrared fluorescence probes, namely, Cy-PL-MPEG, Cy-RRG-PL-MPEG, and Cy-GPICFFRLG-PL-MPEG. Weissleder at paragraph [0138]. In the entire Weissleder disclosure, which admittedly contains a myriad of possibilities with regard to what his probes **can** contain, Applicants could not find a single instance where Weissleder discloses probes that have the specific arrangement now claimed where the specifically recited vectors are attached via a linker (or bond) to a cyanine dye. In sum, even if, for the sake of argument, Weissleder did disclose all of the limitations recited in amended claim 1, which he does not, he does not disclose them arranged or combined in the same way as recited in the claim. Accordingly, Weissleder cannot anticipate claim 1 or the claims that depend therefrom. Reconsideration and withdrawal of the anticipation rejection over Weissleder are therefore respectfully requested.

Turning now to the anticipation rejection over Lauffer, Applicants respectfully point out that Lauffer does not disclose each and every limitation in amended claim 1 and, as a result, cannot anticipate claim 1 or the claims that depend therefrom. Lauffer discloses prodrugs containing an image enhancing (or signal-generating) moiety (IEM); a modification site (MS); and a protein binding moiety (PBM). Lauffer at claim 1 and paragraph [0032]. The PBM is described at length in paragraphs [0065] to [0092] of Lauffer. At paragraphs [0068]-[0070], Lauffer provides that the PBM preferably binds to human serum albumin (HSA), or other proteins in the plasma or interstitial space. Applicants point out, however, that claim 1, as amended, does not recite elements that correspond to, e.g., Lauffer's PBMs. For example, Lauffer does not disclose "moieties that target COX-2, urokinase receptor, epidermal growth factor receptor or vascular endothelial growth factor receptor (VEGFR)" as required by amended claim 1. In addition, Lauffer does not disclose compounds that have the specific arrangement now claimed where the specifically recited vectors are attached via a linker (or bond) to a cyanine dye. Accordingly, Lauffer cannot anticipate claim 1 or the claims that depend therefrom. Reconsideration and withdrawal of the anticipation rejection over Lauffer are therefore respectfully requested.

III. *The rejection of claims 1-9 and 12 under 35 U.S.C. § 103(a) should be withdrawn*

Claims 1-9 and 12 stand rejected under 35 U.S.C. § 103(a) over Klaveness *et al.* (U.S. Patent No. 6,264,914) in view of Lauffer for the reasons set forth on pages 7-10 of the Office Action. Applicants respectfully traverse this rejection to the extent that it might apply to the amended claims.

Klaveness discloses a composition of matter of the formula V-L-R, where V is an organic group having binding affinity for an angiotensin II receptor site; L is a linker moiety or a bond; and R is a moiety detectable in *in vivo* imaging. Klaveness abstract. Klaveness' composition of matter is used to image cardiovascular diseases and disorders. *Id.* The Patent Office itself admits that Klaveness "fails to teach imaging prostate cancer via prostate-specific antigen targeting." Office Action at 8. The Patent Office asserts that Lauffer cures this deficiency in Klaveness because Lauffer teaches prodrug contrast agents comprising, among other components (see discussion above), a modification site (MS) "which is altered by prostate-specific antigen (PSA)." Klaveness at paragraph [0100]. The Patent Office concludes that "[i]t would have been obvious to one of ordinary skill in the art . . . to incorporate [Lauffer's] prostate-specific antigent targeting moiety into Klaveness[']' composition" because PSA is "extremely useful for monitoring therapy, particularly prostatectomy because its presence is decreased to nearly zero following removal of the prostate." Office Action at 10.

In *KSR*, the Supreme Court emphasized that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 82 U.S.P.Q.2d 1385, 1396 (2007). In the instant case, the Patent Office attempts to sustain its obviousness grounds with mere conclusory statements such those presented on page 10 of the Office Action regarding the obviousness of replacing Klaveness' group having binding affinity for an angiotensin II receptor site with an MS disclosed in Lauffer's that is altered by PSA. But, the Patent Office fails to provide the requisite "articulated reasoning" and "rational underpinning" to support its legal conclusion of obviousness. The Patent Office has simply not articulated a reason why one of ordinary skill in the art would consider an organic group having binding affinity for an angiotensin II

receptor site used to image cardiovascular diseases and disorders interchangeable with PSA, which is used to image a completely different disease, namely, prostate cancer. For at least this reason, the Patent Office cannot sustain the rejection of claims 1-9 and 12 over Lauffer in view of Klaveness enunciated in the instant Office Action.

While not acquiescing to the Patent Office's position regarding the patentability of original claims 1-9 and 12, and simply in an effort to expedite the prosecution of the instant application, Applicants have amended claim 1 to recite specific vector moieties and specific reporter moieties, linked to one another in a specific way. Klaveness alone or in combination with Lauffer does not suggest or otherwise contemplate agents such as those claimed in amended claim 1. Accordingly, Klaveness alone or in combination with Lauffer does not render amended claim 1 obvious. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Applicants would like to take this opportunity to respectfully disagree with the Patent Office's statement on page 9 of the Office Action that "Lauffer discloses compounds that are the same as those claimed." As stated above, Lauffer discloses compounds containing an organic group having binding affinity for an angiotensin II receptor site. Those compounds are not the same as the originally claimed compounds, which contain a vector "having affinity for an abnormally expressed biological target associated with prostate cancer." Specific targets are claimed in original claim 5 and include the targets now claimed. Contrary to the Patent Office's position, vectors that target COX-2, urokinase receptor, epidermal growth factor receptor or vascular endothelial growth factor receptor (VEGFR) result in concrete structural differences between the originally claimed agent and the agent now claimed and, as a result, patentably distinguish the claimed invention over the art of record.

IV. *The obviousness-type double patenting rejection should be held in abeyance*

Claims 1-9 and 12 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims of co-pending Appl. Ser. Nos. 10/573,604; 10/573,606; 10/582,680; and 10/582,893.

As an initial matter, Applicants respectfully request that the obviousness-type double patenting rejection be withdrawn with regard to the '604 and the '680 applications because both of those applications stand abandoned. Further, since no claims in the instant application or in the '606 or '893 applications have yet been held allowable, Applicants respectfully ask the Patent Office to hold this rejection in abeyance until the claims in the instant application have been agreed to be otherwise allowable.

In view of the foregoing, it is believed that this application is now in condition for allowance, and a Notice thereof is respectfully requested.

Should the Examiner believe that there are any remaining issues and that consultation might facilitate resolution of these issues, Applicant encourages the Examiner to contact Applicant's undersigned attorney by telephone at 609-514-6905. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

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